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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/587,431 | 07/27/2006 | **Hikaru Kai** | 086039-0015 | 4903 |

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| EXAMINER | |
|---|---|
| BLUMEL, BENJAMIN P | |
| **ART UNIT** | **PAPER NUMBER** |
| 1648 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/587,431 | KAI ET AL. | |
| | Examiner | Art Unit | |
| | BENJAMIN P. BLUMEL | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *5/6/2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-3,7 and 8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 July 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicants are informed that the rejections of the previous Office action not stated below have been withdrawn from consideration in view of the Applicant's arguments. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-3, 7 and 8 are examined on the merits.

### *Response to Arguments*

Applicant's arguments filed 5/6/2010 have been fully considered but they are not persuasive. See responses below.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**(New Rejection Necessitated by Amendments)** Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a New Matter rejection.

The recitation "a polypeptide of about 110,000 Mn having a structure where 13 (Arg Gly Asp SEQ ID NO: 70) sequences and 13 (Gly Ala Gly Ala Gly Ser)9 (SEQ ID NO: 13) sequences (13) are alternately chemically bonded, a polypeptide of about 20,000 Mn having a structure where 5 (Arg Gly Asp SEQ ID NO: 70) sequences and 5

polypeptide of about 10,000 Mn having a structure where 3 (Arg Gly Asp SEQ ID NO: 70) sequences and 3 (Gly Val Pro Gly Val)2 Gly Gly (Gly Ala Gly Ala Gly Ser)3 (SEQ ID NO: 71) sequences (30) are alternately chemically bonded."

Claim 8 is interpreted as being drawn to one protein (i.e., polypeptide (P)) that contains the polypeptides of 110,000 Mn, 20,000 Mn and 10,000 Mn.

Applicant's amendment, filed 5/6/2010, directs to support to page 11, line 27 to page 12, line 9, and asserts that no new matter has been added.

However, the specification as filed does not provide sufficient written description of the above-mentioned limitations. The specification does not provide sufficient support for a single protein containing the above sizes. Therefore, the claims represent a departure from the specification and claims as originally filed.

Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. §112.

Applicant is required to cancel the new matter in the response to this Office Action. Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP §714.02, §2163.05-06 and §2173.05(i).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**(New Rejection Necessitated by Amendments)** Claims 1-3, 7 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites, "…(Y) having a (Gly Ala Gly Ala Gly Ser)b (SEQ ID NO: 56) sequence (wherein b is an integer between 2 to 33, inclusive…), however, since SEQ ID NO: 56 contains 33 "Gly Ala Gly Ala Gly Ser" repeats, it is unclear how SEQ ID NO: 56 can also contain less than 33 such repeats based on the definition for "b" which is an integer between 2 to 33 inclusive. Claims 2, 3, 7 and 8 are rejected since they depend from claim 1.

Claim 8 recites, "…sequences (30) are alternately chemically bonded.", however, it is unclear what "(30)" refers too? Claim 8 also recites, "…sequences (13) are alternately…", however, it is unclear what (13) is referring too?

***Claim Rejections - 35 USC § 103***

**(New Rejection)** Claims 1-3 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sanderson and Smith (Journal of Virology, 1998), Kistner et al. (Developments in Biological Standardization, 1999) and Reiter and Mundt (US PGPub 2003/0108860).

The claimed invention is drawn to a method of improving the viral production in a cell that is attached to a microcarrier via a cell-adhesive protein. The virus is from the family *Flaviviridae, Orthomyxoviridae, Adenoviridae, Herpesviridae, Picornaviridae, Paramyxoviridae, Togaviridae* and *Poxviridae*. The cell adhesive protein comprises that polypeptide (P) having 4 to 50 cell-adhesive minimum amino acid sequences (X) per molecule and 4 to 51 auxiliary amino acid sequences (Y), said auxiliary amino acid sequences (Y) having a (Gly Ala Gly Ala Gly Ser)b sequence, (wherein b is integers of 2 to 33) serving to improve thermal resistance, The adhesive protein is also free from animal-origin components. The method also requires culturing the adhesive cells in a

medium free from animal-origin components; subculturing the cultured adhesive cells using a cell dispersing agent free from animal- origin components; and then inoculating and proliferating a virus in the cells obtained by culturing the adhesive cells.

For purposes of examination, Pronectin F meets the requirements of the claimed cell-adhesion molecule based on page 11 of the specification.

Sanderson and Smith teach the use of several different cellular adhesion molecules in immobilizing cells onto a tissue culture surface. Some adhesion molecules were Pronectin F, fibronectin and collagen II. Sanderson and Smith further utilize these immobilized cells to produce vaccinia virus (of the *Poxviridae* family) in serum containing media. However, Sanderson and Smith do not teach the use of serum-free media in culturing the cells and virus or the use of a microcarrier in culturing cells and virus. *See pages 9926, 9929 and figure 6.*

Kistner et al. teach producing influenza viruses in Vero cells attached to microcarriers (Cytodex-3) which contain denatured collagen (a natural cell binding protein) with serum-free media. Kistner et al. use a porcine trypsin enzyme during the culture process of the virus. Even though collagen is a protein of animal origin, the denatured form of the collagen employed by Kistner et al. is structurally distinct from that of a naturally occurring collagen molecule and therefore not of animal origin. *See pages 103, 106 and table 5.*

Reiter and Mundt teach the culturing of vero cells bound to microcarriers and their culturing in serum-free media. Reiter and Mundt also teach that vaccinia viruses can be cultured in vero cells immobilized on microcarriers. *See paragraphs 33 and 40.*

It would have been obvious to one of ordinary skill in the art to modify the methods taught by Sanderson and Smith in order to improve viral production efficiency by utilizing an attachment protein bound to a microcarrier that immobilizes the cell for which viral replication is intended. One would have been motivated to do so, given the suggestion by Sanderson and Smith that the cell adhesion molecules, such as Pronectin F can be used to immobilize cells that support vaccinia virus replication. There would have been a reasonable expectation of success, given the knowledge that Vero cells which support vaccinia virus replication can be immobilized on microcarriers with an inserted cell adhesion molecule, as taught by Kistner et al., and also given that knowledge that vero cells can be immobilized on microcarriers and cultured in serum free media and these cells can also be used in culturing vaccinia virus, as taught by Reiter and Mundt. Thus the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

**Response to Arguments:**

Applicants argue that Kistner et al., Wang and Ouyang, Aerts et al., nor Kobatake et al. teach the claimed cell adhesion polypeptide that now requires a (Gly Ala Gly Ala Gly Ser) sequence. Applicants state that this sequence provides for improve stability (i.e., thermal resistance) and higher production of virus.

In response, based on the teachings of Sanderson and Smith, the Pronectin F employed in their analysis of vaccinia virus production meets the requirements for the presently claimed cell adhesion polypeptide since such a protein contains the required (Gly Ala Gly Ala Gly Ser) sequence (see page 11 of specification).

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BENJAMIN P. BLUMEL whose telephone number is (571)272-4960. The examiner can normally be reached on M-F, 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/BENJAMIN P BLUMEL/
Examiner
Art Unit 1648